Relationship Between Low Cardiorespiratory Fitness and Mortality in Normal-Weight, Overweight, and Obese Men

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Context Recent guidelines for treatment of overweight and obesity include recommendations for risk stratification by disease conditions and cardiovascular disease (CVD) risk factors, but the role of physical inactivity is not prominent in these recommendations.

Objective To quantify the influence of low cardiorespiratory fitness, an objective marker of physical inactivity, on CVD and all-cause mortality in normal-weight, overweight, and obese men and compare low fitness with other mortality predictors.

Design Prospective observational data from the Aerobics Center Longitudinal Study.

Setting Preventive medicine clinic in Dallas, Tex.

Participants A total of 25 714 adult men (average age, 43.8 years [SD, 10.1 years]) who received a medical examination during 1970 to 1993, with mortality follow-up to December 31, 1994.

Main Outcome Measures Cardiovascular disease and all-cause mortality based on mortality predictors (baseline CVD, type 2 diabetes mellitus, high serum cholesterol level, hypertension, current cigarette smoking, and low cardiorespiratory fitness) stratified by body mass index.

Results During the study period, there were 1025 deaths (439 due to CVD) during 258 781 man-years of follow-up. Overweight and obese men with baseline CVD or CVD risk factors were at higher risk for all-cause and CVD mortality compared with normal-weight men without these predictors. Using normal-weight men without CVD as the referent, the strongest predictor of CVD death in obese men was baseline CVD (age- and examination year-adjusted relative risk [RR], 14.0; 95% confidence interval [CI], 9.4-20.8); RRs for obese men with diabetes mellitus, high cholesterol, hypertension, smoking, and low fitness were similar and ranged from 4.4 (95% CI, 2.7-7.1) for smoking to 5.0 (95% CI, 3.6-7.0) for low fitness. Relative risks for all-cause mortality in obese men ranged from 2.3 (95% CI, 1.7-2.9) for men with hypertension to 4.7 (95% CI, 3.6-6.1) for those with CVD at baseline. Relative risk for all-cause mortality in obese men with low fitness was 3.1 (95% CI, 2.5-3.8) and in obese men with diabetes mellitus 3.1 (95% CI, 2.3-4.2) and as slightly higher than the RRs for obese men who smoked or had high cholesterol levels. Low fitness was an independent predictor of mortality in all body mass index groups after adjustment for other mortality predictors. Approximately 50% (n = 1674) of obese men had low fitness, which led to a population-attributable risk of 39% for CVD mortality and 44% for all-cause mortality. Baseline CVD had population attributable risks of 51% and 27% for CVD and all-cause mortality, respectively.

Conclusions In this analysis, low cardiorespiratory fitness was a strong and independent predictor of CVD and all-cause mortality and of comparable importance with that of diabetes mellitus and other CVD risk factors.

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Between 1976 and 1980 to 1988 and 1994, the prevalence of obesity in the United States increased substantially, from 14.5% to 22.5%.[1] In 1998, the US National Institutes of Health (NIH) and the World Health Organization published guidelines for the treatment of obesity.[2,3] In these reports, overweight and obesity are defined, and treatment guidelines are provided for physicians. It is recommended that clinicians first classify patients by body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, with overweight defined as a BMI of 25.0 to 29.9 kg/m^2 and obesity as a BMI of at least 30.0 kg/m^2. Further stratification of risk is recommended by considering the presence of coexisting disease and cardiovascular disease (CVD) risk factors.

The NIH guidelines specify that obese persons with established CVD or type 2 diabetes mellitus (DM) are at "very high risk" for death and that patients with 3 or more CVD risk factors are "at high absolute risk."[2] Physical inactivity and serum triglyceride levels of more than 2.3 mmol/L (>200 mg/dL) are mentioned as "other risk factors" that indicate "incremental absolute risk above that estimated from the preced-

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ing risk factors."[2] However, quantitative risk estimates are not available for these other risk factors.

It is well established that active individuals have high levels of cardiorespiratory fitness, and in controlled experimental trials, increases in exercise result in increases in fitness.[4-7] Cardiorespiratory fitness can be measured objectively in a laboratory and thereby provides quantifiable data that are a reliable marker of habitual physical activity. In this study, we provide quantitative risk estimates that make it possible to compare and contrast the presence of established disease, established CVD risk factors, and low cardiorespiratory fitness as they relate to CVD and all-cause mortality in normal-weight, overweight, and obese men.

METHODS

Patient Data

This study is based on data from the Aerobics Center Longitudinal Study (ACLS), an observational study of patients examined at a preventive medicine clinic in Dallas, Tex, from 1970 to 1993. The study has been reviewed and approved annually by the Cooper Institute Institutional Review Board. Study participants come to the clinic for periodic health examinations and counseling about diet, exercise, and other lifestyle factors associated with increased risk of chronic disease. Many participants are sent by their employers for the examination, some are referred by their personal physicians, and others are self-referred. We excluded patients with a history of cancer at baseline, those with a BMI of less than 18.5 kg/m^2 at the baseline examination, those younger than age 20 at baseline, and those with less than 1 year of follow-up.

Patients came for the examination after an overnight fast of at least 12 hours and gave their informed consent to participate in the examination and the follow-up study. Patients completed an extensive self-report of demographic characteristics, personal and family health history, and health habits, including a history of smoking and physical activity questionnaire. Patients underwent a physical examination by a physician. Trained technicians using procedures described in a detailed manual of operations conducted all examinations,[8-11] which included measuring height, weight, and blood pressure[12]; determining cardiorespiratory fitness by administering a maximal exercise test on a treadmill; and drawing blood for blood chemistry analysis. Lipid and fasting plasma glucose levels were determined by automated techniques in the Cooper Clinic laboratory, which participates in and meets quality control standards of the Centers for Disease Control and Prevention Lipid Standardization Program.

We determined cardiorespiratory fitness using a maximal exercise test on a treadmill.[13] Patients began walking at 88 m/min at no elevation. At the end of the first minute, elevation was increased to 2% and thereafter increased 1% per minute until the 25th minute. For the few subjects who were able to continue beyond 25 minutes, elevation remained constant and speed was increased at each subsequent minute by 5.4 m/min. The exercise electrocardiogram was monitored continuously and blood pressure was obtained every 5 minutes. Patients continued the test to the limits of volitional fatigue. Total time of the test correlates highly (0.92) with measured maximal oxygen uptake, and we calculated maximal metabolic equivalents (METs) attained during the test (1 MET = resting metabolic rate, defined as an oxygen uptake of 3.5 mL $\times$ kg^{-1} $\times$ min^{-1}).[14]

The principal method of mortality surveillance was through the National Death Index, which has established validity and has been used widely in population-based cohort studies.[15] Nosologists coded the death certificates according to the *International Classification of Diseases, Ninth Revision* for both the underlying cause and up to 4 contributing causes of death.

Statistical Analyses

This study uses all-cause and CVD mortality (*International Classifications of Diseases, Ninth Revision,* codes 390-449) as the outcome variables. The principal exposure variable for this report was body habitus. We assigned the men to 1 of 3 BMI categories using criteria from guidelines for the evaluation and treatment of obesity[2,3]: normal weight (BMI, 18.5-24.9 kg/m^2), overweight (BMI, 25.0-29.9 kg/m^2), or obese (BMI $\geq$30.0 kg/m^2). We calculated mortality rates for BMI strata by the presence or absence of 6 mortality predictors.

Two of the mortality predictors were disease conditions. Baseline CVD was ascertained by the medical history, physical examination, and exercise test. The definition of baseline CVD was previous myocardial infarction, stroke, myocardial revascularization, abnormal electrocardiogram at rest or during the exercise test, or failure to achieve at least 85% of a patient's age-predicted maximal heart rate during the exercise test. Some patients were unable to continue the exercise test to exhaustion. In other cases, physicians may have stopped the exercise test early due to untoward signs or symptoms. Individuals with early test termination for any of these reasons would have their cardiorespiratory fitness underestimated and would be more likely than other patients to be classified as having low fitness. The reasons for early test termination also are likely to be associated with baseline chronic disease, which could lead to early mortality. Therefore, our conservative approach was to include these patients in the baseline CVD group. The second disease condition used as an exposure variable was type 2 DM, defined as a history of physician-diagnosed type 2 DM or having fasting plasma glucose levels of at least 7.0 mmol/L ($\geq$126 mg/dL).

The other 4 exposure variables were CVD risk factors: high serum cholesterol levels, defined as serum cholesterol higher than 6.2 mmol/L (>240 mg/dL); hypertension, defined as a history of physician-diagnosed hypertension or blood pressure of at least 140/90 mm Hg; current cigarette smoking; and low cardiorespiratory fitness (maximal MET cut points for low fitness in

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Table 1. Baseline Characteristics, Amount of Follow-up, and Deaths by Body Mass Index Groups in 25 714 Men: Aerobics Center Longitudinal Study*

Characteristics	Body Mass Index Category, kg/m²		
	Normal Height (18.5-24.9)	Overweight (25.0-29.9)	Obese (≥30)
No. of subjects	10 623	11 798	3293
Man-years of observation	112 114	117 639	29 028
No. of deaths	367	500	158
No. of cardiovascular disease deaths	126	237	76
Age, y†	42.5 (10.3)	44.7 (9.8)	44.5 (8.5)
Exercise tolerance, METs†	12.5 (2.2)	11.2 (1.9)	9.7 (1.7)
Body mass index, kg/m²†	23.2 (1.3)	27.0 (1.4)	33.2 (3.7)
Total cholesterol level, mmol/L [mg/dL]†	5.3 (1.2) [205.0 {46.4}]	5.6 (1.1) [217.0 {43.0}]	5.8 (1.1) [224.2 {43.0}]
Triglyceride level, mmol/L [mg/dL]†	1.2 (1.3) [106.2 {115.0}]	1.7 (1.6) [150.4 {142.0}]	2.3 (1.7) [204.0 {150.4}]
Diastolic blood pressure, mm Hg†	78.6 (9.1)	81.5 (9.4)	85.5 (9.8)
Systolic blood pressure, mm Hg†	119.3 (13.5)	122.1 (13.6)	126.5 (13.8)
Alcohol use, g/wk†	152.6 (275.2)	186.8 (312.3)	182.8 (335.0)
Current cigarette smoking, %	15.8	20.0	20.3
Physically inactive, %‡	28	38	50
Hypertension, %	17.1	26.2	41.6
Diabetes mellitus, %	3.0	4.7	10.0
Parental cardiovascular disease, %	24.7	28.0	28.8
Prevalent cardiovascular disease, %§	9.1	12.7	16.5

*All tests for homogeneity across body mass index groups were significant at $P<.05$. MET indicates metabolic equivalent.
†Values are presented as mean (SD).
‡Men reporting no leisure-time physical activity in the 3 months before the examination.
§History of cardiovascular disease, abnormal electrocardiogram at rest or during the exercise test, or low maximal exercise heart rate.

each group were 20-39 years, 10.5; 40-49 years, 9.9; 50-59 years, 8.8; and ≥60 years, 7.5). We used cut points for the other quantitative exposure variables that have been recommended previosly.[2,3,16-18]

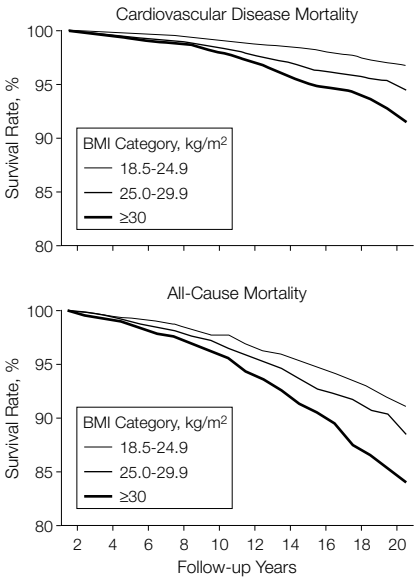
We used Cox partial likelihood methods to provide point estimates and 95% confidence interval (CI) estimates[19] adjusted for the covariables (age, examination year, and parental history of CVD) and other mortality predictors. All reported *P* values are 2-sided. We first calculated crude and net survival curves for the 3 BMI categories. We calculated age- and examination year-adjusted CVD and all-cause mortality rates for the 3 BMI categories. We then performed cross-tabulation analyses of age- and examination year-adjusted mortality rates using the BMI categories and the presence or absence of the primary exposure variables. We repeated these cross-tabulations with additional adjustment for parental history of CVD and each of the other exposures. We also calculated multivariate-adjusted population-attributable risks (PAR) as p_c (1-1/RR), where p_c is the proportion of exposed decedents and relative risk (RR) is the adjusted RR for the exposure.[20] Note that adjusted PARs for separate factors do not sum to the adjusted PAR for the combined factors,[21] unless these factors are mutually exclusive.[22]

RESULTS

The study population included 25 714 men followed up for approximately 10 years, for a minimum of 1 year.

Baseline characteristics of study participants by BMI categories are shown in TABLE 1. The population is homogeneous, with more than 95% white and about 80% college graduates. Most of the subjects were executives and professionals. Prevalence rates for normal weight, overweight, and obesity were 41%, 46%, and 13%, respectively. Men who were overweight or obese were more likely than the normal-weight men to have baseline disease, smoke cigarettes, be sedentary, and

Figure. Survival Curves for Cardiovascular Disease and All-Cause Mortality by Body Mass Index (BMI) Categories



Data are from 25 714 men with 1025 all-cause deaths and 439 cardiovascular disease deaths during 258 781 man-years of observation.

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have a family history of CVD. Overweight and obese men also had less favorable levels of clinical and health habit variables than normal-weight men.

During the follow-up period, there were 1025 deaths (439 due to CVD) during the 258 781 man-years of follow-up. Survival curves for CVD and all-cause mortality by BMI category are presented in the FIGURE. Obese men had a 2.6 times higher risk for CVD (95% CI, 2.0-3.6) and a 1.9 times higher risk for all-cause mortality (95% CI, 1.5-2.3), after adjustments were made for age and examination year compared with normal-weight men. Overweight men had intermediate death rates between normal-weight and obese men. The age- and examination year-adjusted RR for CVD and all-cause mortality (calculated by cross-tabulating categories of BMI and presence or absence of other exposure variables and using the referent category of normal-weight men who did not have the specific mortality predictor) are shown in TABLE 2. Obese men with CVD at baseline had a higher risk for CVD mortality and all-cause mortality than did normal-weight men with no history of CVD. Results of the analyses for DM, hypertension, elevated cholesterol levels, current smoking, and low-cardiorespiratory fitness showed similar patterns of risk for each of these

Table 2. Age- and Examination Year-Adjusted Relative Risk (RR) of Cardiovascular Disease and All-Cause Mortality by Body Mass Index (BMI) and Other Mortality Predictors in 25 714 Men*

	Normal Weight†		Overweight†		Obese†	
Mortality Predictor	No. of Deaths (No. of Men)	RR (95% CI)	No. of Deaths (No. of Men)	RR (95% CI)	No. of Deaths (No. of Men)	RR (95% CI)
Cardiovascular Deaths (n = 439)						
Cardiovascular disease						
No	54 (9653)	1.0 (referent)	110 (10 306)	2.0 (1.5-2.8)	29 (2750)	2.6 (1.6-4.0)
Yes	72 (970)	6.9 (4.8-8.9)	127 (1492)	8.1 (6.4-12.3)	47 (543)	14.0 (9.4-20.8)
Type 2 diabetes mellitus						
No	106 (10 301)	1.0 (referent)	190 (11 242)	1.7 (1.4-2.2)	52 (2962)	2.5 (1.8-3.4)
Yes	20 (322)	2.2 (1.4-3.6)	47 (556)	3.9 (2.8-5.6)	24 (331)	4.9 (3.2-7.7)
Cholesterol levels						
≤6.2 mmol (≤240 mg/dL)	89 (9002)	1.0 (referent)	137 (8821)	1.6 (1.2-2.1)	38 (2332)	2.1 (1.4-3.1)
>6.2 mmol (>240 mg/dL)	37 (1621)	1.4 (0.9-2.0)	100 (2977)	2.8 (2.1-3.7)	38 (961)	4.7 (3.2-6.8)
Hypertension						
No	63 (8800)	1.0 (referent)	126 (8706)	2.1 (1.6-2.9)	35 (1923)	3.4 (2.2-5.1)
Yes	63 (1823)	2.6 (1.9-3.8)	111 (3092)	3.4 (2.5-4.6)	41 (1370)	4.5 (3.0-6.6)
Current smoker						
No	93 (8942)	1.0 (referent)	173 (9446)	1.8 (1.4-2.4)	56 (2623)	2.9 (2.0-4.0)
Yes	33 (1681)	2.1 (1.4-3.1)	64 (2352)	3.3 (2.4-4.5)	20 (670)	4.4 (2.7-7.1)
Low fitness						
No	81 (9636)	1.0 (referent)	113 (9505)	1.5 (1.1-2.0)	16 (1619)	1.6 (1.0-2.8)
Yes	45 (987)	3.1 (2.2-4.5)	124 (2293)	4.5 (3.4-6.0)	60 (1674)	5.0 (3.6-7.0)
All-Cause Deaths (n = 1025)						
Cardiovascular disease						
No	243 (9653)	1.0 (referent)	307 (10 306)	1.3 (1.1-1.5)	86 (2750)	1.7 (1.3-2.1)
Yes	124 (970)	2.7 (2.1-3.3)	193 (1492)	3.0 (2.5-3.7)	72 (543)	4.7 (3.6-6.1)
Type 2 diabetes mellitus						
No	328 (10 301)	1.0 (referent)	415 (11 242)	1.2 (1.0-1.4)	114 (2962)	1.7 (1.4-2.1)
Yes	39 (322)	1.5 (1.1-2.1)	85 (556)	2.4 (1.9-3.1)	44 (331)	3.1 (2.3-4.2)
Cholesterol levels						
≤6.2 mmol (≤240 mg/dL)	277 (9002)	1.0 (referent)	317 (8821)	1.2 (1.0-1.4)	88 (2332)	1.5 (1.2-1.9)
>6.2 mmol (>240 mg/dL)	90 (1621)	1.1 (0.9-1.4)	183 (2977)	1.7 (1.4-2.0)	70 (961)	2.7 (2.1-3.5)
Hypertension						
No	233 (8800)	1.0 (referent)	277 (8706)	1.3 (1.1-1.5)	82 (1923)	2.1 (1.6-2.7)
Yes	134 (1823)	1.6 (1.3-2.0)	223 (3092)	1.9 (1.6-2.3)	76 (1370)	2.3 (1.7-2.9)
Current smoker						
No	283 (8942)	1.0 (referent)	369 (9446)	1.3 (1.1-1.5)	113 (2623)	1.8 (1.5-2.3)
Yes	84 (1681)	1.7 (1.3-2.1)	131 (2352)	2.1 (1.7-2.5)	45 (670)	3.0 (2.2-4.2)
Low fitness						
No	265 (9636)	1.0 (referent)	279 (9505)	1.1 (1.0-1.3)	35 (1619)	1.1 (0.8-1.5)
Yes	102 (987)	2.2 (1.8-2.8)	221 (2293)	2.5 (2.1-3.0)	123 (1674)	3.1 (2.5-3.8)

*Patients with a BMI of 18.5 to 24.9 kg/m^2 and without the mortality predictor served as the referent group for each analysis. Patients who were younger than 20 years, had a history of cancer, or had a BMI of less than 18.5 kg/m^2 were excluded from the analysis.
†Normal weight is defined as a BMI of 18.5 to 24.9; overweight, 25.0 to 29.9; and obese, at least 30.0 kg/m^2.

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other risk predictors. When compared with the referent category, men with the other mortality predictors had a steep direct gradient of risk across BMI categories.

We repeated the analyses presented in Table 2 with additional adjustment for parental history of CVD and each of the other exposure variables (data not shown). The pattern of results was similar to those in Table 2, although RRs were attenuated with the multivariate adjustment. However, each of the exposure variables remained significantly associated with mortality in the overweight and obese men. We also repeated the analyses in Table 2 for 2 groups of men, those followed up for less than 10 years and those followed up for 10 or more years. The results from each of these analyses (data not shown) were similar to those presented in Table 2.

There were substantial differences in the prevalence of the mortality predictors in overweight and obese men. For example, for the 3293 obese men, low fitness was the most common predictor with a prevalence rate about 5 times higher than that of DM, which was the least common predictor. Hypertension had the highest prevalence in normal-weight and overweight men. The multivariate-adjusted RRs and number of men with each of the mortality predictors for each BMI category, along with the PAR for both CVD and all-cause mortality, are shown in TABLE 3. We performed a separate series of analyses in each BMI stratum and calculated multivariate-adjusted RRs for each mortality predictor. The referent category for each of these analyses was the group of men within that BMI stratum who did not have the specific mortality predictor.

From the perspective of an individual patient, presence of CVD at baseline is the strongest predictor of death in all BMI strata, although low fitness is similar to baseline CVD as a mortality predictor in obese men. From a population perspective, baseline CVD has the highest PAR in normal-weight men, and CVD and low fitness have comparable PARs in overweight and obese men.

COMMENT

Overweight and obesity are prevalent in the United States and in many other countries.[1-3] In the cohort of well-educated men examined in this study, 46% were overweight and 13% were obese, which is similar to percentage rates for a representative sample of US men.[1] When compared with normal-weight men in our study, obese men had an almost 3-fold higher risk of CVD mortality and a 2-fold higher risk of all-cause mortality. These rates are comparable to other studies.[23,24] The principal purpose of our study was to evaluate low cardiorespiratory fitness as a quantifiable high-risk characteristic in normal-weight, overweight, and obese men and to compare its effect on mortality with that of other risk indicators described in the obesity treatment guidelines.[2,3] Although cardiorespiratory fitness has a genetic component, which explains 25% to 40% of the variation in fitness,[25,26] it is clear that habitual physical activity is the other major determinant of fitness, and fitness is improved in most individuals with appropriate exercise participation.[4-7]

Data presented in this article support the hypothesis that low cardiorespiratory fitness adds to overweight and obesity in influencing mortality adversely. The strongest predictor of mortality in our data was baseline CVD, which was expected. All other characteristics that we evaluated (DM, elevated cholesterol levels, hypertension, current cigarette smoking, and low fitness) were comparable predictors of mortality in both overweight and obese men. Overweight men with any of the mortality predictors other than CVD

Table 3. Multivariate Adjusted Relative and Population Attributable Risks (PAR) of Cardiovascular Disease and All-Cause Mortality by Body Mass Index (BMI) Categories and Other Characteristics in 25 714 Men*

	Normal Weight†			Overweight†			Obese†		
		RR (95% CI) [PAR, %]‡			RR (95% CI) [PAR, %]‡			RR (95% CI) [PAR, %]‡	
Mortality Predictor	No. of Men	Cardiovascular Disease Death	All-Cause Mortality	No. of Men	Cardiovascular Disease Death	All-Cause Mortality	No. of Men	Cardiovascular Disease Death	All-Cause Mortality
Baseline cardiovascular disease	845	4.6 (3.1-6.8) [45]	2.3 (1.8-2.9) [19]	1267	3.5 (2.6-4.7) [38]	2.0 (1.6-2.4) [19]	543	5.8 (3.5-9.7) [51]	2.4 (1.7-3.5) [27]
Diabetes mellitus	322	1.5 (0.9-2.4) [5]	1.3 (0.9-1.8) [2]	556	1.7 (1.2-2.3) [8]	1.6 (1.3-2.0) [6]	331	1.9 (1.1-3.1) [15]	1.5 (1.1-2.2) [9]
High cholesterol levels	1621	1.2 (0.8-1.7) [5]	1.0 (0.8-1.3) [0]	2977	1.6 (1.2-2.1) [16]	1.3 (1.1-1.6) [8]	961	2.1 (1.3-3.3) [26]	1.7 (1.2-2.3) [18]
Hypertension	1823	2.1 (1.4-3.0) [26]	1.5 (1.2-1.9) [12]	3092	1.4 (1.1-1.8) [13]	1.4 (1.2-1.7) [13]	1370	1.4 (0.9-2.3) [15]	1.1 (0.8-1.4) [4]
Current smoker	1681	1.7 (1.2-2.6) [11]	1.4 (1.1-1.8) [7]	2352	1.6 (1.2-2.3) [10]	1.5 (1.2-1.9) [9]	670	1.3 (0.8-2.3) [6]	1.5 (1.0-2.1) [9]
Low fitness	987	1.7 (1.1-2.5) [15]	1.6 (1.3-2.1) [10]	2293	1.9 (1.4-2.5) [25]	1.7 (1.4-2.0) [18]	1674	2.0 (1.2-3.6) [39]	2.3 (1.5-3.4) [44]

*Diabetes mellitus is for subjects with a history of diabetes or who had baseline fasting plasma glucose of at least 7.0 mmol/L (≥126 mg/dL); high cholesterol levels, higher than 6.2 mmol/L (>240 mg/dL); hypertension, a history of hypertension or baseline blood pressure of higher than 140/90 mm Hg; low fitness, the least fit 20% in each age group; current smoker, a self-report of smoking at the baseline examination; and baseline cardiovascular disease, a history of myocardial infarction, stroke, or revascularization or an abnormal resting or exercise electrocardiogram (including a maximal exercise heart rate <85% of the age-predicted value). Normal weight is defined as a BMI of 18.5 to 24.9; overweight, 25.0 to 29.9; and obese, at least 30.0 kg/m^2.

†Of the 10 623 men in the normal-weight group, 367 died with 126 due to cardiovascular disease; of the 11 798 men in the overweight group, 500 died with 237 due to cardiovascular disease; and of the 3293 men in the obese group, 158 died, with 76 due to cardiovascular disease.

‡Relative risks (RRs) and PARs are adjusted for age, examination year, BMI as a continuous variable, parental history of cardiovascular disease, and all other characteristics in the table. The referent category for each attributable risk analysis includes men in a specific BMI stratum who did not have the particular mortality predictor. CI indicates confidence interval.

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had about a 3-fold higher CVD death rate and a 2-fold higher all-cause death rate when compared with normal-weight men without the condition. Obese men with any one of the other characteristics other than baseline CVD had CVD death rates about 5-fold higher and all-cause death rates about 3-fold higher than in normal-weight men without the characteristic.

Low cardiorespiratory fitness was a strong predictor of mortality in our cohort, with RRs comparable with, if not greater than, the RRs for DM, high cholesterol levels, hypertension, and current cigarette smoking (Table 2 and Table 3). Our findings suggest that it is as important for a clinician to assess an obese patient's fitness status as it is to measure fasting plasma glucose and cholesterol levels, evaluate blood pressure, and inquire about smoking habits. We recognize that many, if not most, primary care physicians may not have an exercise testing laboratory and that the cost of such measurements exceed those needed for obtaining blood lipid and glucose levels and measuring blood pressure. However, there is an extensive network of community facilities such as health clubs or YMCAs and YWCAs that offer fitness testing services performed by well-trained exercise clinicians for a modest cost.

If fitness testing is not feasible, we encourage clinicians to evaluate their patients' physical activity habits. This is probably important for all patients, but in view of our results, it is essential for overweight and obese patients. For example, the Physician Assisted Counseling for Exercise program includes simple scales to assess patients' activity patterns and their motivational readiness to become more active,[27,28] and the program's efficacy has been confirmed. A behaviorally based, lifestyle, physical activity, counseling approach, in which sedentary individuals are encouraged to integrate more activity into their daily routines, by climbing stairs, taking short walks, and generally increasing daily activity, has been shown to be effective over a 2-year period.[29-31]

PAR estimates for any characteristic are based on several assumptions and must be interpreted carefully. However, overweight or obese patients with baseline CVD have substantially increased risk for death, although the RRs for low fitness presented in Table 3 are nearly as high as they are for CVD. From a public health perspective, low fitness, with its high prevalence, also should receive attention. About 50% of the obese men in our study were unfit, whereas 16% had baseline CVD and 10% had DM. The prevalence of these conditions was 19%, 11%, and 5%, respectively, in overweight men. The PAR for all-cause mortality in obese men underscores the importance of low fitness. If the association between fitness and mortality is causal and if all obese unfit men in our cohort had been fit, there might have been as many as 44% fewer deaths among obese men in our study. If none of these men had CVD at baseline, there might have been as many as 27% fewer deaths. In overweight men, the PARs for all-cause mortality were comparable for low fitness and prevalent CVD.

Our study has several strengths. Our data on cardiorespiratory fitness are determined by a maximal exercise test on a treadmill, and the fitness data provide quantitative risk estimates. We also have laboratory measurements of CVD risk factors, which provide objective data on the other mortality predictors included in this report, and an extensive physical examination, which allows for thorough evaluation of the presence or absence of baseline disease. Our large sample size allowed us to perform cross-tabulation analyses to evaluate the various risk predictors by BMI strata and to analyze data in 2 follow-up intervals.

A limitation of our study is that it included only men, because we do not yet have enough deaths in the women in our cohort to perform analyses similar to those reported herein. However, in our previous reports on fitness in which we have been able to perform parallel analyses in men and women, results are generally similar.[8] We also have few members of minority groups in our cohort, and the men in our study are primarily from mid- to upper-socioeconomic strata, so generalization to other groups should be done with caution. We only have baseline data on fitness, other exposures, and weight, so we do not know if changes in any of these variables occurred during follow-up or from the influence of possible changes on the results.

In conclusion, low cardiorespiratory fitness is as important as type 2 DM and other CVD risk factors as a predictor of CVD mortality and all-cause mortality in overweight or obese men. Clinicians should evaluate fitness in their patients just as they now obtain a medical history and measure blood pressure and cholesterol and plasma glucose levels. Evaluating fitness, or at least physical activity, allows for more complete risk stratification in overweight and obese patients and can enhance clinical decision making.

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The scientist takes off from the manifold observations of predecessors, and shows his intelligence, if any, by his ability to discriminate between the important and the negligible, by selecting here and there the significant steppingstones that will lead across the difficulties to new understanding. The one who places the last stone and steps across to the terra firma of accomplished discovery gets all the credit. Only the initiated know and honor those whose patient integrity and devotion to exact observation have made the last step possible.

—Hans Zinsser (1878-1940)

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